

A circular black ink stamp. The text "OIPE" is at the top, "JCB88 OFFICE" is on the right, "PATENT &amp; TRADEMARK" is at the bottom, and "JAN 31 2000" is in the center.

**BOX PCT**

In re:	International Patent Application of Douglas E. Kligman <i>et al.</i>	: Authorized Officer: : J. Venkat :
International Appln. No.:	PCT/US97/01919	: : :
International Filing Date:	05 February 1997 (05.02.97)	: : :
For:	COMPOSITION AND METHOD FOR EFFECTING SUPERFICIAL CHEMICAL SKIN PEELS	: : Attorney Docket : No. 6149-29 PC

This is in response to the Written Opinion of the ~~PEA/US~~ <sup>US</sup>, dated 17 October 1997. Applicants request reconsideration of the statement in the Written Opinion that claims 15-19 lack novelty under PCT Article 33(2) and that claims 1-14 and 20-22 lack an inventive step under PCT Article 33(3).

The Authorized Officer has stated that claims 15-19 are anticipated by Henderson, U.S. Patent 5,296,476 and that claims 1-14 and 20-22 lack an inventive step as being obvious over the combination of Brody, "Chemical Peeling," Mosby Year Book, Inc., St. Louis, MO, pp. 53-73 (1992) and Henderson.

The Authorized Officer has commented that Applicants' claims 15-19 lack novelty since Henderson discloses compositions comprising salicylic acid, ethanol and bentonite (thickening agent) at column 4, lines 15-20, and discloses a salicylic acid range of 2-50% by weight at column 3, lines 60-61. Henderson in fact does not teach or suggest Applicants' concentrated salicylic acid compositions for use in chemical skin peeling techniques. Applicants' composition claims 15-19 are directed to a composition useful in superficial chemical skin peels that *consists essentially of* specific ingredients that do *not* include the "synergistic combination of calcium citrate and salicylic acid" taught by Henderson (column 1, lines 46-47).

Henderson describes a variety of skin care compositions having calcium citrate and

salicylic acid as the active ingredients, and these formulations are described as "creams, masques, ointments, emulsions, lotions, gels, soaps, soap-free medication cleansing bars and the like" (column 1, line 54-59). The skin care formulation with the highest concentration of salicylic acid described by Henderson is a hard corn remover (column 4, lines 21-25) which contains 10-40 wt% micronized calcium citrate, 10-20 wt% salicylic acid, 30% ethyl alcohol, 5% bentonite (a well-known colloidal clay thickener) and the remainder (5-45 wt%) water. Contrary to the Authorized Officer's assertion, there do not appear to be any disclosures by Henderson of salicylic acid-containing formulations containing more than 20 wt% salicylic acid.

The hard corn remover formulation of Henderson differs from Applicants' claimed composition in significant respects: (i) the micronized calcium citrate component in the Henderson hard corn remover must be present in an amount of 10-40 wt%, which is far in excess of the amount of dermatologically acceptable adjuvants specified in Applicants' claimed composition, namely, about 0.01 to about 5 wt%; and (ii) the very poor water solubility of the calcium citrate results in this skin care formulation being a thick dispersion of suspended solids, in contrast to Applicants' claimed composition which is a concentrated salicylic acid solution. The Henderson reference therefore fails to teach Applicants' claimed concentrated salicylic acid compositions useful for superficial skin peels, since each and every element set forth in Applicants' claims is not expressly or inherently described in the cited reference.

Applicants' contention that their concentrated salicylic acid composition is patentably different from the Henderson skin care formulations is demonstrated by the experimental results described in the accompanying Declaration of Dr. Douglas Kligman, which demonstrates that the hard corn remover formulation of Henderson, a suspension of calcium citrate, salicylic acid and bentonite is ineffective as a superficial chemical skin peel.

The enclosed Declaration of Dr. Douglas Kligman describes the preparation of the hard corn remover formulation of Henderson's Example 1 (column 4, lines 15-20) and its use to treat subjects having photodamaged skin. Four formulations of the Henderson hard corn remover were preparing containing representative values of micronized calcium citrate (10 wt% and 40 wt%) and salicylic acid (15 wt% and 20 wt%). The two values selected for calcium citrate represent the upper and lower limits of this component in the Henderson hard corn remover formulation, and the two values selected for salicylic acid represent the maximum amount and mid-range amount for this component in the Henderson hard corn remover formulations. The value of 15 wt% salicylic acid also represents the lower limit of salicylic acid specified for the present invention.

As described in the Declaration of Dr. Douglas Kligman, the protocol described in Applicants' specification at pages 16-17 was followed to treat six subjects with moderately photodamaged skin. As described in the Declaration, the Henderson formulations were found to be completely ineffective for improving the skin condition of the treated subjects. There was no peeling noted and no change in the texture or quality of the skin for the subjects treated.

By contrast, subjects whose facial skin was treated with the three Kligman formulations containing 25 wt%, 20 wt% and 15 wt% salicylic acid solutions in ethanol exhibited skin desquamation at the 48-72-hour examination, indicating that peeling of the treated skin had begun.

The results described in this Declaration underscore the fact that Applicants' claimed concentrated salicylic acid compositions are patentably different from the skin care formulations described in the Henderson reference. Applicants' claims 15-19 therefore meet the requirement for novelty set out in PCT Article 33(2), as well as the standard for inventive step in PCT Article 33(3).

With respect to the rejection of claims 1-14 and 20-22 as being obvious over the combination of the Brody article and Henderson, the Authorized Officer has commented that Brody teaches that salicylic acid has been used as an agent for chemical skin peeling and that although Brody does not teach the combination of solvent and salicylic acid claimed in the present application, Henderson teaches the use of salicylic acid with alcohol for skin care compositions.

The shortcomings described above of Henderson as a reference against Applicants' claimed invention are equally applicable to the present rejection of claims 1-14 and 20-22.

Brody at page 60 teaches only that salicylic acid in dilute concentrations, *i.e.*, 3-5% has been a mainstay in dermatologic therapy and that salicylic acid alone is ordinarily not strong enough to act as an adequate wounding agent for chemical peeling. Brody also mentions the use by Swinehart of a 50% salicylic acid ointment, which is *not* salicylic acid dissolved in a solvent, to treat the hands and forearms of patients. A detailed discussion of this prior art technique and its disadvantages is provided in Applicants' specification, in the "Background of the Invention" section at page 3, line 15 to page 4, line 2. The Brody teachings concerning salicylic acid consequently fail to suggest use of a concentrated salicylic acid solution in a chemical skin peel technique.

Henderson, as described above, does not teach or suggest the use of concentrated salicylic acid solutions in chemical skin peeling techniques, and the Henderson

skin care compositions containing micronized calcium citrate and salicylic acid are not described as useful for chemical skin peeling.

Even if it is assumed, solely for the sake of argument, that the combination of the Brody article with Henderson might possibly suggest Applicants' claimed invention, the unexpected and superior results provided by Applicants' claimed superficial chemical skin peeling method using a concentrated salicylic acid solution clearly rebuts any presumption of obviousness. These results were described above and are reported in the enclosed Declaration of Dr. Douglas Kligman.

The experimental results described in the Kligman Declaration demonstrate that Applicants' claimed concentrated salicylic acid composition and its method of use in chemical skin peeling provides unexpected and superior results that are unobvious over the combined teachings of Henderson and the Brody article.

For all of these reasons, Applicants' claims 15-19 define an invention that is both novel and inventive over the teachings of Henderson. Likewise, Applicants' claims 1-14 and 20-22 define an invention that is unobvious and provide an inventive step over the teachings of Brody and Henderson.

Applicants' claims 1-22 are novel under PCT Article 33(2) and define an inventive step under PCT Article 33(3). The Authorized Officer is respectfully requested to reconsider the conclusion in the Written Opinion regarding novelty and inventive step and to issue an International Preliminary Examination Report that indicates that the claimed subject matter is novel, involves an inventive step and is industrially applicable.

Respectfully submitted,

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17 December 1997

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Enclosure